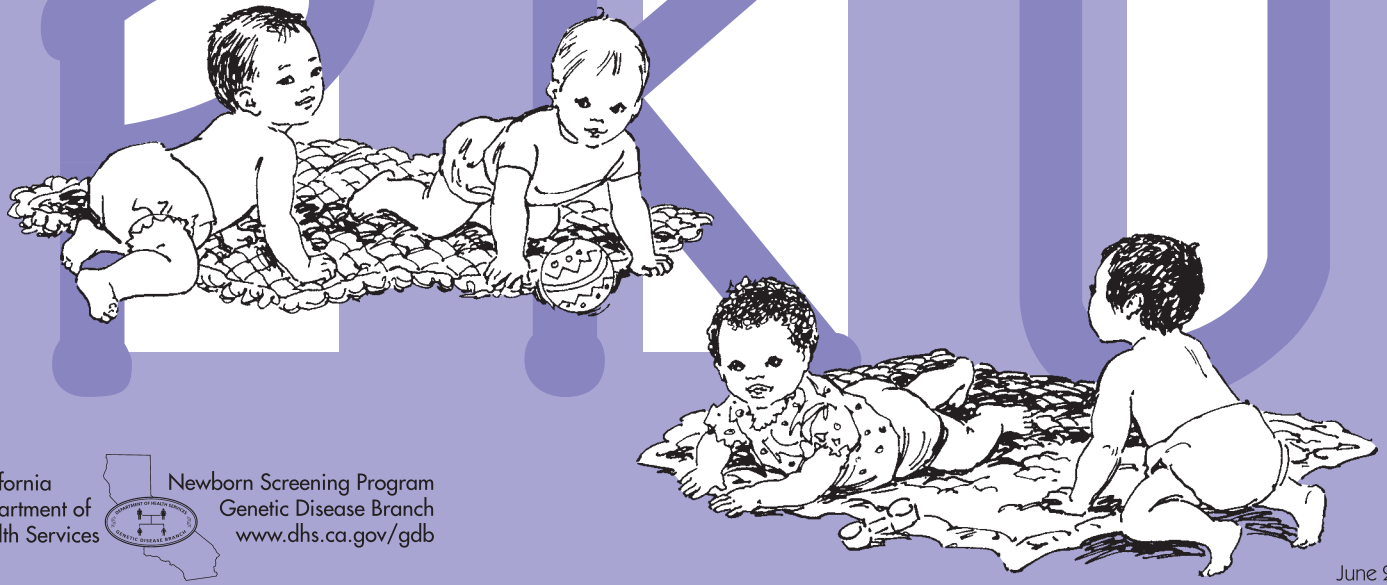
Parents' Guide to PKU

Phenylketonuria



California
Department of
Health Services

Newborn Screening Program
Genetic Disease Branch
www.dhs.ca.gov/gdb

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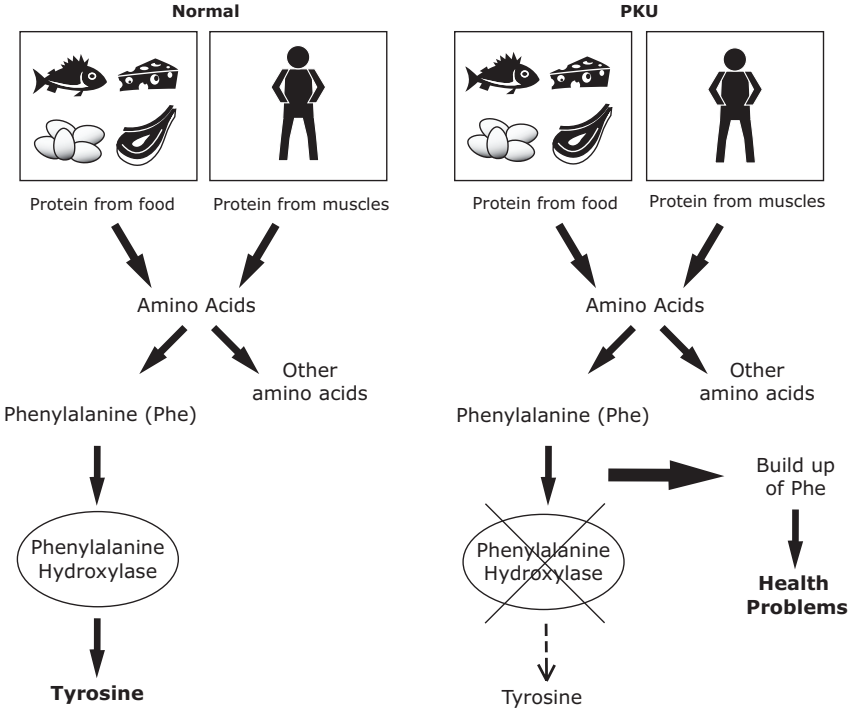
The information in this booklet is general and is not meant to be specific to each child with PKU. Certain treatments may be recommended for some children but not others. Children with PKU should be followed by a physician specializing in metabolic diseases (metabolic specialist) in addition to their primary doctor. For a list of metabolic centers, see page 16 or visit our website at www.dhs.ca.gov/gdb.

*Underlined words in booklet are defined in the Glossary

What is PKU?

PKU stands for “phenylketonuria.” It is one type of amino acid disorder. People with these disorders have problems breaking down amino acids from the protein in the food they eat. With PKU, people have problems breaking down a specific amino acid called phenylalanine.



What causes PKU?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

PKU occurs when an enzyme, called “phenylalanine hydroxylase” (PAH), is either missing or not working properly. This enzyme’s job is to break down the amino acid phenylalanine (Phe – pronounced ‘fee’). When a child with PKU eats food containing Phe, it builds up in the blood and causes problems. Phe is found in almost every food, except pure fat and sugar.

What causes the PAH enzyme to be missing or not working correctly?

Genes tell the body to make various enzymes. People with PKU have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the PAH enzyme either does not work properly or is not made at all.

If PKU is not treated, what problems occur?

Babies with PKU seem perfectly normal at birth. The first effects are usually seen around 6 months of age. Untreated infants may be late in learning to sit, crawl and stand. They may pay less attention to things around them. Without treatment, a child with PKU will develop progressive brain damage. In addition, some of the effects of untreated PKU include:

- mental retardation
- seizures
- behavior problems
- hyperactivity
- restlessness or irritability
- a skin condition called eczema
- a “musty” or “mousy” body odor
- fair hair and skin

What happens when PKU is treated?

Children with PKU who start treatment soon after birth and keep their Phe levels within the suggested range usually have normal growth and intelligence. Some children, even when treated, have problems with school work and may need extra help.

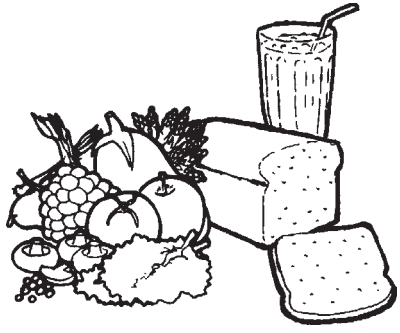
If treatment is not started until several weeks after birth, delays or learning problems may occur. The level of delay varies from child to child.

Children who start treatment after 6 months of age are often mentally retarded. Treatment is still important, even if started late, because it can help control behavior and mood problems and prevent further damage to the brain.

What is the treatment for PKU?

Prompt treatment is needed to prevent mental retardation. Newborns need to drink a special medical formula. It may still

be possible to breastfeed your baby as long as you get help from a dietician with experience in treating PKU. The amount of breast milk needs to be carefully monitored. Babies who are breastfed usually need the medical formula as well.



Most children with PKU need to eat a special diet made up of very low-protein foods, special medical foods, and the special formula. You must start the low-Phe diet as soon as you know your child has PKU.

Your baby's primary doctor will work with a metabolic specialist and a dietician to adjust your child's diet. Your dietician will create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. The diet should be continued throughout life.

The following pages describe the treatments often advised for children with PKU.

1. Tracking Phe levels

Babies and young children with PKU need to have regular blood tests to measure their Phe levels. If there is too much or too little Phe in the blood, the diet and formula may need to be adjusted.

Monitoring of Phe level in the blood is an important part of PKU treatment. The Newborn Screening Program offers Phe monitoring through the State Genetic Disease lab to all individuals with PKU seen at CCS-approved Metabolic Special Care Centers in California. There is no charge for this service. The Metabolic Center staff will provide you with more information on this testing.

2. Medical formula

Even though they need less Phe, children with PKU – like all children – still need a certain amount of protein. The medical formula gives babies and children with PKU the nutrients and protein they need while helping keep their Phe levels within a safe range.

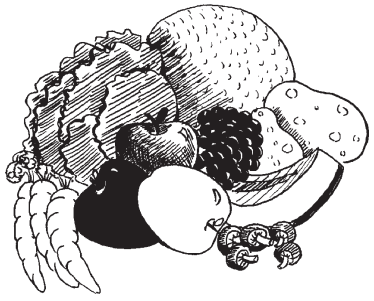
Your metabolic specialist and dietician will tell you what type of formula is best and how much to use.

3. Low-Phe food plan

The low-Phe diet is made up of foods that are very low in Phe. This means your child must not have cow's milk, regular formula, meat, fish, eggs or cheese. Regular flour, dried beans, nuts, and peanut butter also have Phe and must be avoided or strictly limited.

It is very important that your child avoid the sugar substitute aspartame (sold under the brand names "Equal," Nutrasweet," "Sweetmate," and "Canderal"). Aspartame contains high amounts of Phe. It can quickly raise the blood levels of Phe in people with PKU. Your child must not have any diet foods or drinks that contain aspartame.

Many vegetables and fruits have only small amounts of Phe and can be eaten in carefully measured amounts. In addition, there are other medical foods such as low-Phe flours, baking mixes, breads, and pastas that are made especially for people with PKU.



Your child's food plan will depend on many things such as his or her age, weight, general health, and blood test results. Your dietician will fine-tune your child's diet over time.

Your child should follow this diet throughout life. Adults who do not stay on the diet and have high levels of Phe in their blood may notice some of the following:

- trouble paying attention
- problems making good decisions
- slow thinking
- irritability
- eczema

Are There Special Concerns for Women With PKU Considering Pregnancy?

Women with PKU must be on the low-Phe diet **before** becoming pregnant. They need to stay on the diet throughout pregnancy. If they are not on the low-Phe diet when they become pregnant, they have a high chance of having babies with birth defects, mental retardation, and/or learning problems.

Women who are not on the diet usually have high levels of Phe in their blood. The extra Phe gets to the fetus and causes problems with brain and body growth. Babies of untreated mothers may have the following:

- small brains
- mental retardation
- birth defects of the heart
- low birth weight

This condition is called “maternal PKU syndrome.”

Women with PKU who want to have children need to have very low blood Phe levels before they get pregnant. During pregnancy, they need to:

- stay on the low-Phe diet
- visit their PKU clinic on a regular basis
- have their blood Phe levels checked often

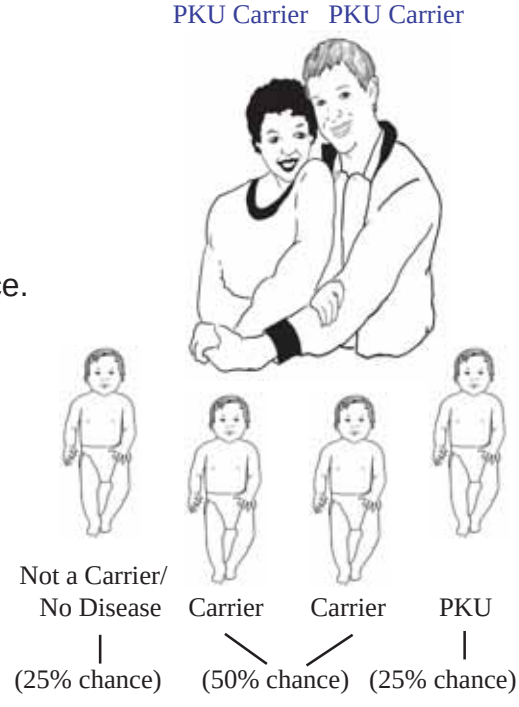
How is PKU inherited?

PKU affects both boys and girls equally.

Everyone has a pair of genes that make the PAH enzyme. In children with PKU, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent. This is called autosomal recessive inheritance.

Parents of children with PKU rarely have the disorder. Instead, each parent has a single non-working gene for PKU. They are called carriers. Carriers are not affected because their other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have two working genes. This means the child is not a carrier and does not have the disease. There is a 50% chance for the child to be a carrier, just like the parents. There is a 25% chance for the child to have PKU.



Chances apply to each pregnancy

Genetic counseling is available to families who have children with PKU. Genetic counselors can answer your questions about how PKU is inherited, options during future pregnancies, and how to test other family members. Other family members can also ask about genetic counseling and testing for PKU.

Is genetic testing available?

Genetic testing is not necessary to diagnose your child. It can be helpful for carrier or prenatal testing.

Genetic testing for PKU can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause PKU.

What other testing is available?

PKU is confirmed by measuring the amount of Phe in a blood sample. Talk to your doctor or your genetic counselor if you have questions about testing for PKU.

Can you test during pregnancy?

If both gene changes are known in your child with PKU, DNA testing can be done during future pregnancies to determine if the sibling also has PKU. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have PKU or be carriers?

If they are healthy and developing normally, older brothers and sisters of a baby with PKU are unlikely to have PKU. Talk to your doctor or genetic counselor if you have questions about your other children.

When both parents are known PKU carriers or have had a baby with PKU, subsequent newborns should have special diagnostic testing in addition to the newborn screen to test for PKU.

Brothers and sisters of the baby who do not have PKU still have a chance to be carriers like their parents. Carriers do not have the disorder and will never develop it.

Each of the parents' brothers and sisters has a chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with PKU.

How many people have PKU?

About 25 babies are born in California each year with PKU.
PKU happens in people of all ethnic groups around the world.
However, it is generally more common in Caucasians.

Does PKU go by any other names?

PKU is sometimes also called:

- Classical PKU
- hyperphenylalaninemia or hyperphe
- phenylalanine hydroxylase deficiency

RESOURCES

PKU Parents of California
PMB 117, 9785 Baseline Road
Rancho Cucamonga, CA 91730
(909) 466-4688
www.pkunetwork.org

Children's PKU Network
3790 Via De La Valle, Ste. 120
Del Mar, CA 92014
(800) 377-6677

National Coalition for PKU and Allied Disorders
PO Box 1244
Mansfield, MA 02048
www.pku-allieddisorders.org

California Department of Health Services
Genetic Disease Branch
Newborn Screening Program
www.dhs.ca.gov/gdb

METABOLIC CENTERS

Cedars-Sinai Medical Center
(310) 423-9914

Children's Hospital Central California
(559) 353-6400

Children's Hospital & Research Center at Oakland
(510) 428-3550

Children's Hospital of Los Angeles
(323) 660-2450

Children's Hospital of Orange County
(714) 532-8852

Children's Hospital & Health Center
(619) 543-7800

Harbor/UCLA Medical Center
(310) 222-3756

Kaiser Permanente Medical Center, No. Cal.
(510) 752-7703

Kaiser Permanente Medical Center, So. Cal.
(323) 783-6970

Los Angeles County/ USC Medical Center
(323) 226-3816

Lucile Salter Packard Children's Hospital at Stanford
(650) 723-6858

Sutter Medical Center
(916) 733-6023

UC Davis Medical Center
(916) 734-3112

UC San Francisco Medical Center
(415) 476-2757

UC Los Angeles Medical Center
(310) 206-6581

UC Irvine Medical Center
(714) 456-8513

GLOSSARY

Amniocentesis - Test done during pregnancy (usually between 16 and 20 weeks). A needle is used to remove a small sample of fluid from the sac around the fetus. The sample can be used to test for certain genetic disorders in the fetus.

Autosomal recessive - Autosomal recessive conditions affect both boys and girls equally. How autosomal recessive inheritance works: Everyone has a pair of genes responsible for making each enzyme in the body. A person with a metabolic disorder has one enzyme that is either missing or not working properly. The problem is caused by a pair of "recessive" genes that are not working correctly. They do not make the needed enzyme. A person has to have two non-working "recessive" genes in order to have an autosomal recessive metabolic disorder. A person with an autosomal recessive disorder inherits one non-working gene from their mother and the other from their father.

Carrier - A person who has a gene mutation in one of their genes that cause a disease, but does not have any symptoms of the disease themself. The mutation is often recessive, which means that both copies of the gene have to be mutated in order for disease symptoms to develop. Carriers are able to pass the mutation

onto their children and therefore have an increased chance of having a child with the disease.

Classical PKU - The two major types of PKU are Classical PKU and Hyperphe. Classical PKU is the more serious type of PKU in which there is a complete block in the breakdown of phe to tyrosine. People with this type of PKU are treated with a low phe diet and special formula.

CVS - Chorionic Villus Sampling (CVS) is a special test done during early pregnancy (usually between 10 and 12 weeks). A small sample of the placenta is removed for testing. This sample can be used to test for certain genetic disorders in the fetus.

DNA - Deoxyribonucleic acid (DNA) is a molecule that makes up chromosomes. It is composed of four units (called bases) that are designated A, T, G, and C. The sequence of the bases spell out instructions for making all of the proteins in an organism. The instructions set for each individual protein is a gene. A change in one of the DNA letters making up a gene is a mutation. In some cases, these mutations can alter the protein instructions and lead to disease. Each individual passes their chromosomes on to their children, and therefore pass down the DNA

instructions. It is these instructions that cause certain traits, such as eye or hair color, to be inherited.

Enzyme - A molecule that helps chemical reactions take place. For example, enzymes in the stomach speed up the process of breaking down food. Each enzyme can participate in many chemical reactions without changing or being used up.

Gene - A segment of DNA that contains the instructions to make a specific protein (or part of a protein). Genes are contained on chromosomes. Chromosomes, and the genes on those chromosomes, are passed on from parent to child. Errors in the DNA that make up a gene are called mutations and can lead to diseases.

Genetic Counseling - Genetic counseling gives patients and their families education and information about genetic-related conditions and helps them make informed decisions. It is often provided by Genetic Counselors or Medical Geneticists who have special training in inherited disorders.

Hyperphe - A condition in which the PKU gene is only mildly affected so the person can still convert 5-10% of phe into tyrosine (unlike Classical PKU where the person is unable to convert any phe). In general, hyperphe patients are not treated unless the phe builds up to high levels in their body.

Phenylalanine - One of 20 amino acids that make up protein. It is also called “phe.” It is not made by the body and must be eaten in the diet. It is found in all foods that contain protein.

Seizures - These are also called “convulsions” or “fits”. During a seizure, a person loses consciousness and control of their muscles. It may also cause involuntary movements. Seizures can happen for many reasons. Some causes are metabolic disorders, a metabolic crisis, brain injury, and infection.

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